

*Anderson et al.
Serial No.: 09/941,626
Page 5 of 8*

REMARKS

Claims 1-14, 16 and 59 are pending. Claims 15, 17-58 and 60-62 have been canceled without prejudice. Claims 63-68 are new. Support for the amendments is found throughout the specification. Reconsideration of the rejection is respectfully requested.

Claims 1-14, 16 and 59 were rejected under 35 USC 112, second paragraph as being indefinite by lacking antecedent basis for "plural nucleic acids". Claim 1 has been amended to recite that the phrase refers to the sequenced nucleic acids.

Claim 1 was also considered vague and indefinite by the word "complementary". Specifically, the examiner wishes to know whether this refers to 100% complementarity or a lower number such as complementarity for hybridization probing purposes. Neither choice is appropriate given the usage in the specification.

While complementarity is ideally complete, in practice certain "errors" result during the method. While reverse transcribing an RNA, it is possible for the reaction to be incomplete, particularly for very long RNA molecules, thereby truncating the cDNA. Likewise, PCR amplification as a general process occasionally introduces an error. The specification recites using random primers that may result in annealing with a mismatch, which would introduce a point mutation in one of the strands.

On the other hand, hybridization probing purposes may involve relatively low levels of complementarity. Under less stringent conditions one can obtain a heteroduplex with little homology. The present invention does not envision such low amounts of complementarity, which would prevent accurate identification of the virus. A high degree of complementarity is needed and applicants do not intend a definition of complementarity that renders the claimed method inoperable.

Claims 1, 2, 7-12, 14, 16 and 59 were rejected under 35 USC 112, first paragraph as being enabling for identifying by comparing the sequence to a sequence database, but not for any generic identity determination. This rejection is respectfully traversed.

One need not perform a direct comparison to a sequence database of known sequences to determine the identity of the infectious particle. One may easily use a microarray with immobilized oligonucleotides and make a determination based on the

Anderson et al.
Serial No.: 09/941,626
Page 6 of 8

pattern of array sites hybridized. See the specification page 24, second paragraph. This is indirectly a measurement of sequences by comparing the hybridization pattern with a database of hybridization patterns of known viruses etc. This may even be used as a sequencing technique as stated in the specification on page 11, first paragraph. Clearly, the microarray industry is well established for identifying nucleic acids based on hybridization to a microarray. This established field for determining gene sequences, mutations, polymorphisms, RNA expression, etc. is clearly enabled without undue experimentation. Thus, the rejection's contention that such could not be so used in the present invention is unfounded.

Furthermore, applicants' previous patents, a representative one discussed on page 5, second paragraph, determine the virus based on the restriction enzyme fragment map of an isolated virus. That patent, which was incorporated by reference, may compare restriction enzyme maps for identification. Note that restriction enzyme fragment map comparisons are a well-known method for viral, plasmid and other nucleic acid determinations. In the present invention, the determined sequence can be used to generate a restriction enzyme fragment map for the infectious particle for comparison to other such maps for virus (or other infectious particle) identification. See the specification page 19, first paragraph, particularly the last sentence. In this situation, comparison is to a different database, not just that of claim 3. Accordingly, the rejection has been overcome and its withdrawal is respectfully requested.

Claims 1, 3, 4, 6, 7, 9, 10, 12, 13 and 59 were rejected under 35 USC 102(b) as being clearly anticipated by Reyes et al. The examiner urges that Reyes et al purifies viral particles, extracts the nucleic acids, clones and sequences nucleic acids and uses probes with these sequences to assay for the virus. This rejection is respectfully traversed.

Several differences are present in the claimed invention, which are neither disclosed nor suggested in Reyes et al. Claim 1 lines 1-2 recite "A method for identifying a plurality of infectious particles in a sample..." Note the term "plurality of infectious particles". Reyes et al apparently purifies only one virus particle, namely post-transfusion, non-A, non-B hepatitis virus (PT NANB). Reyes et al identifies only one virus, not the "particles" (plural form) from the "plural sequenced nucleic acids" (Claim 1 last paragraph). Reyes et

*Anderson et al.
Serial No.: 09/941,626
Page 7 of 8*

al appears to have extracted and partially sequenced nucleic acids from only one virus. The selection step Reyes et al uses with antibodies in column 15, lines 7-11 for all examples should select for clones from only the one virus. This is contrary to the present invention and prevents one from isolating nucleic acids for sequencing "at least two nucleic acids" as recited in claim 1, fourth paragraph.

Furthermore, claim 1 recites "determining the identity of the infectious particles from the sequence or by overlapping sequences derived from plural nucleic acids". Reyes et al does not determine the identity of their single viral particle from sequencing. Reyes et al start with known positive samples from known infected patients, experimental animals or cell cultures. The determination that this was PT NANB hepatitis virus was already done before attempting to separate the virus. By contrast the present claims recite determining the identity of the infectious particle after and as a result of sequencing. Thus, Reyes et al is not performing the claimed steps. In the preferred embodiment of the present invention one has pooled serum from human patients containing an unknown number of viruses (including zero), where one must first perform most of the claimed method before one can be "determining the identity of the infectious particle..." as claimed.

Other claims contain features not disclosed or appreciated by Reyes et al. For Example claims 3 and 13 compare the sequence of the nucleic acids to a database of known sequences. The rejection refers to column 3, lines 4-16 as showing such a comparison. This comparison is between different isolates of the post-transfusion non-A, non-B hepatitis virus. This comparison includes comparing a known virus to other known related or identical viruses of the same type. This is a comparison to each other within the few samples in Reyes et al possession and the sample in another publication. Most people would not consider this a disclosure of or a teaching for "a comparison to a database". Regardless, this is not a comparison to "known infectious particles" (plural form) as recited in Claim 13. At best, Reyes et al can be said to compare their sequences to one other and that assumes you accept the tortured definition of "database" to include one element.

Claim 6 recites "plural new infectious particles are simultaneously detected". Contrary to the claims, none of the experiments performed by Reyes et al simultaneously detects more than one of anything. Reyes et al identifies only one new virus (PT NANB

*Anderson et al.
Serial No.: 09/941,626
Page 8 of 8*

hepatitis virus) starting with samples believed to contain only that virus. Nothing in Reyes et al suggest that they sought to identify plural new infectious particles.

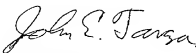
Claim 59 recites a containment system. Reyes et al does not appear to use any special containment system at all. Accordingly, for all of these rejections should be withdrawn.

CONCLUSIONS

In view of the amendments and comments above, the rejections have been overcome. Reconsideration, withdrawal of the rejections and early indication of allowance are respectfully requested. If any issues remain, the examiner is encouraged to telephone the undersigned.

If needed, applicants petition for an extension of time under the provisions of 37 CFR 1.136(a) for sufficient time to accept this response. The commissioner hereby is authorized to charge payment of any fees under 37 CFR § 1.17, which may become due in connection with the instant application or credit any overpayment to Deposit Account No.500933.

Respectfully submitted,



John E. Tarcza
Reg. No. 33,638

Date: February 4, 2004

John E. Tarcza
Intellectual Property Advisor
Large Scale Biology Corporation
20451 Seneca Meadows Parkway
Germantown, MD 20876
301-354-1200 ext. 1223
301-354-1300 Fax.
E-MAIL: john.tarcza@lsbc.com